RECOMBIVAX HB- hepatitis b vaccine (recombinant) injection, suspension
A-S Medication Solutions

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use RECOMBIVAX HB safely and effectively. See full prescribing information for RECOMBIVAX HB.

RECOMBIVAX HB® Hepatitis B Vaccine (Recombinant)
Suspension for intramuscular injection
Initial U.S. Approval: 1986

INDICATIONS AND USAGE

RECOMBIVAX HB is a vaccine indicated for prevention of infection caused by all known subtypes of hepatitis B virus. RECOMBIVAX HB is approved for use in individuals of all ages. RECOMBIVAX HB Dialysis Formulation is approved for use in predialysis and dialysis patients 18 years of age and older. (1)

DOSAGE AND ADMINISTRATION

RECOMBIVAX HB

- Persons from birth through 19 years of age: A series of 3 doses (0.5 mL each) given on a 0-, 1-, and 6-month schedule. (2.1)
- Adolescents 11 through 15 years of age: A series of either 3 doses (0.5 mL each) given on a 0-, 1-, and 6-month schedule or a series of 2 doses (1.0 mL) on a 0- and 4- to 6-month schedule). (2.1)
- Persons 20 years of age and older: A series of 3 doses (1.0 mL each) given on a 0-, 1-, and 6-month schedule. (2.1)

RECOMBIVAX HB Dialysis Formulation

- Adults on predialysis or dialysis: A series of 3 doses (1.0 mL each) given on a 0-, 1-, and 6-month schedule. (2.1)

DOSAGE FORMS AND STRENGTHS

RECOMBIVAX HB is a sterile suspension available in the following presentations:

- 0.5 mL (5 mcg) Pediatric/Adolescent Formulation single-dose vials and prefilled syringes (3, 11, 16.1)
- 1 mL (10 mcg) Adult Formulation single-dose vials and prefilled syringes (3, 11, 16.1)

RECOMBIVAX HB Dialysis Formulation is a sterile suspension available in the following presentation:

- 1 mL (40 mcg) single-dose vials (3, 11, 16.1)

CONTRAINDICATIONS

Severe allergic or hypersensitivity reactions (e.g., anaphylaxis) after a previous dose of any hepatitis B-containing vaccine, or to any component of RECOMBIVAX HB, including yeast. (4, 11)

WARNINGS AND PRECAUTIONS

The vial stopper, the syringe plunger stopper, and tip cap contain dry natural latex rubber which may cause allergic reactions in latex-sensitive individuals. (5.1)
Apnea following intramuscular vaccination has been observed in some infants born prematurely. Decisions about when to administer an intramuscular vaccine, including RECOMBIVAX HB, to infants born prematurely should be based on consideration of the individual infant's medical status and the potential benefits and possible risks of vaccination. (5.2)

ADVERSE REACTIONS

In healthy infants and children (up to 10 years of age), the most frequently reported systemic adverse reactions (>1% injections), in decreasing order of frequency, were irritability, fever, diarrhea, fatigue/weakness, diminished appetite, and rhinitis. (6.1)
In healthy adults, injection site reactions and systemic adverse reactions were reported following 17% and 15% of the injections, respectively. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., at 1-877-888-4231 or VAERS at 1-800-822-7967 or www.vaers.hhs.gov.

DRUG INTERACTIONS

Do not mix RECOMBIVAX HB with any other vaccine in the same syringe or vial. (7.1)
See 17 for PATIENT COUNSELING INFORMATION.

Revised: 6/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

RECOMBIVAX HB® [Hepatitis B Vaccine, Recombinant] is indicated for prevention of infection caused by all known subtypes of hepatitis B virus. RECOMBIVAX HB is approved for use in individuals of all ages. RECOMBIVAX HB Dialysis Formulation is approved for use in adult predialysis and dialysis patients 18 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular administration. See Section 2.2 for subcutaneous administration in persons with hemophilia.

RECOMBIVAX HB should be administered as soon as possible after being removed from refrigeration *[see How Supplied/Storage and Handling (16)]*.

2.1 Dosage and Schedule

RECOMBIVAX HB:

Persons from birth through 19 years of age: A series of 3 doses (0.5 mL each) given on a 0-, 1-, and 6-month schedule.

Adolescents 11 through 15 years of age: A series of 3 doses (0.5 mL each) given on a 0-, 1-, and 6-month schedule or a series of 2 doses (1.0 mL each) on a 0- and 4- to 6-month schedule.

Persons 20 years of age and older: A series of 3 doses (1.0 mL each) given on a 0-, 1-, and 6-month schedule.

RECOMBIVAX HB Dialysis Formulation:

Adults on predialysis and dialysis: A series of 3 doses (1.0 mL each) given on a 0-, 1-, and 6-month schedule.

Table 1 summarizes the dose and formulation of RECOMBIVAX HB for specific populations, regardless of the risk of infection with hepatitis B virus.

Table 1: RECOMBIVAX HB Recommended Dose and Administration Schedules

Group	Dose/Regimen
Infants*, Children and Adolescents 0-19 years of age (Pediatric/Adolescent Formulation)	5 mcg (0.5 mL) 3 doses at 0, 1, and 6 months
Adolescents†	10 mcg‡ (1.0 mL)

11 through 15 years of age (Adult Formulation)	10 mcg‡ (1.0 mL) 2 doses at 0 and 4-6 months
Adults ≥20 years of age (Adult Formulation)	10 mcg‡ (1.0 mL) 3 doses at 0, 1, and 6 months
Predialysis and Dialysis Patients§ (Dialysis Formulation)	40 mcg (1.0 mL) 3 doses at 0, 1, and 6 months

* For specific recommendations for infants see ACIP recommendations.{1}
† Adolescents (11 through 15 years of age) may receive either regimen: 3 × 5 mcg (Pediatric Formulation) or 2 × 10 mcg (Adult Formulation).
‡ If the suggested dose (10 mcg) is not available, the appropriate dosage can be achieved with two 5 mcg doses. However, the Dialysis Formulation may be used only for adult predialysis/dialysis patients.
§ See also recommendations for revaccination of predialysis and dialysis patients in *[Dosage and Administration (2.4)]*.

2.2 Preparation and Administration

Shake the single-dose vial or single-dose prefilled syringe well to obtain a slightly opaque, white suspension before withdrawal and use. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Discard if the suspension does not appear homogeneous or if extraneous particulate matter remains or if discoloration is observed.

For single-dose vials, withdraw and administer entire dose of RECOMBIVAX HB intramuscularly using a sterile needle and syringe. Discard vial after use.

For single-dose prefilled syringes, securely attach a needle by twisting in a clockwise direction and administer dose of RECOMBIVAX HB intramuscularly. Discard syringe after use.

The deltoid muscle is the preferred site for intramuscular injection for adults, adolescents and children 1 year of age and older whose deltoid is large enough for intramuscular injection. The anterolateral aspect of the thigh is the preferred site for intramuscular injection for infants younger than 1 year of age. RECOMBIVAX HB should not be administered in the gluteal region, as injections given in the buttocks have resulted in lower seroconversion rates than expected.{2}

RECOMBIVAX HB may be administered subcutaneously to persons at risk for hemorrhage following intramuscular injections (e.g., hemophiliacs). However, hepatitis B vaccines are known to result in lower antibody response when administered subcutaneously.{3} Additionally, when other aluminum-adsorbed vaccines have been administered subcutaneously, an increased incidence of local reactions including subcutaneous nodules has been observed. Therefore, consider subcutaneous administration only in persons who are at risk of hemorrhage following intramuscular injections.

Do not administer intravenously or intradermally.

2.3 Known or Presumed Exposure to Hepatitis B Virus

Known or Presumed Exposure to HBsAg

Refer to recommendations of the Advisory Committee on Immunization Practices (ACIP) and to the package insert for hepatitis B immune globulin (HBIG) for management of persons with known or presumed exposure to the hepatitis B virus (e.g., neonates born of infected mothers or persons who experienced percutaneous or permucosal exposure to the virus). When recommended, administer RECOMBIVAX HB and HBIG intramuscularly at separate sites (e.g., opposite anterolateral thighs for exposed neonates) as soon as possible after exposure. Administer additional doses of RECOMBIVAX HB (to complete a vaccination series) in accordance with ACIP recommendations.

2.4 Booster Vaccinations

The duration of the protective effect of RECOMBIVAX HB in healthy vaccinees is unknown at present and the need for booster doses is not yet defined. The ACIP provides recommendations for use of a booster dose or revaccination series in previously vaccinated individuals with known or presumed exposure to Hepatitis B Virus.

Consider a booster dose or revaccination with RECOMBIVAX HB Dialysis Formulation (blue color code) in predialysis/dialysis patients if the anti-HBs level is less than 10 mIU/mL at 1 to 2 months after the third dose. Assess the need for a booster dose annually by antibody testing, and give a booster dose when the anti-HBs level declines to less than 10 mIU/mL.{3}

3 DOSAGE FORMS AND STRENGTHS

RECOMBIVAX HB is a sterile suspension available in the following presentations:

- 0.5 mL (5 mcg) Pediatric/Adolescent Formulation single-dose vials and prefilled syringes
- 1 mL (10 mcg) Adult Formulation single-dose vials and prefilled syringes

RECOMBIVAX HB DIALYSIS FORMULATION is a sterile suspension available in the following presentation:

- 1 mL (40 mcg) single-dose vial *[see Description (11) and How Supplied/Storage and Handling (16)]*

4 CONTRAINDICATIONS

Do not administer RECOMBIVAX HB to individuals with a history of severe allergic or hypersensitivity reactions (*e.g.*, anaphylaxis) after a previous dose of any hepatitis B-containing vaccine or to any component of RECOMBIVAX HB, including yeast *[see Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity to Latex

The vial stopper and the syringe plunger stopper and tip cap contain dry natural latex rubber, which may cause allergic reactions in latex-sensitive individuals.

5.2 Apnea in Premature Infants

Apnea following intramuscular vaccination has been observed in some infants born prematurely. Decisions about when to administer an intramuscular vaccine, including RECOMBIVAX HB, to infants born prematurely should be based on consideration of the individual infant's medical status and the potential benefits and possible risks of vaccination. For RECOMBIVAX HB, this assessment should include consideration of the mother's hepatitis B antigen status and the high probability of maternal transmission of hepatitis B virus to infants born to mothers who are HBsAg positive if vaccination is delayed.

5.3 Infants Weighing Less Than 2000 g

Hepatitis B vaccination should be delayed until 1 month of age or hospital discharge in infants weighing <2000 g if the mother is documented to be HBsAg negative at the time of the infant's birth. Infants weighing <2000 g born to HBsAg positive or HBsAg unknown mothers should receive vaccine and hepatitis B immune globulin (HBIG) in accordance with ACIP recommendations if HBsAg status cannot be determined{3} *[see Dosage and Administration (2)].*

5.4 Prevention and Management of Allergic Vaccine Reactions

Appropriate medical treatment and supervision must be available to manage possible anaphylactic reactions following administration *[see Contraindications (4)].*

5.5 Limitations of Vaccine Effectiveness

Hepatitis B virus has a long incubation period. RECOMBIVAX HB may not prevent hepatitis B infection in individuals who have an unrecognized hepatitis B infection at the time of vaccination. Additionally, vaccination with RECOMBIVAX HB may not protect all individuals.

6 ADVERSE REACTIONS

In healthy infants and children (up to 10 years of age), the most frequently reported systemic adverse reactions (>1% injections), in decreasing order of frequency, were irritability, fever, diarrhea, fatigue/weakness, diminished appetite, and rhinitis. In healthy adults, injection site reactions and systemic adverse reactions were reported following 17% and 15% of the injections, respectively.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

In three clinical studies, 434 doses of RECOMBIVAX HB, 5 mcg, were administered to 147 healthy infants and children (up to 10 years of age) who were monitored for 5 days after each dose. Injection site reactions and systemic adverse reactions were reported following 0.2% and 10.4% of the injections, respectively. The most frequently reported systemic adverse reactions (>1% injections), in decreasing order of frequency, were irritability, fever (≥101°F oral equivalent), diarrhea, fatigue/weakness, diminished appetite, and rhinitis.

In a study that compared the three-dose regimen (5 mcg) with the two-dose regimen (10 mcg) of RECOMBIVAX HB in adolescents, the overall frequency of adverse reactions was generally similar.

In a group of studies, 3258 doses of RECOMBIVAX HB, 10 mcg, were administered to 1252 healthy adults who were monitored for 5 days after each dose. Injection site reactions and systemic adverse reactions were reported following 17% and 15% of the injections, respectively. The following adverse reactions were reported:

Incidence Equal To or Greater Than 1% of Injections

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS

Injection site reactions consisting principally of soreness, and including pain, tenderness, pruritus, erythema, ecchymosis, swelling, warmth, nodule formation.

The most frequent systemic complaints include fatigue/weakness; headache; fever (≥100°F); malaise.

GASTROINTESTINAL DISORDERS

Nausea; diarrhea

RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS

Pharyngitis; upper respiratory infection

Incidence Less Than 1% of Injections

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS

Sweating; achiness; sensation of warmth; lightheadedness; chills; flushing

GASTROINTESTINAL DISORDERS

Vomiting; abdominal pains/cramps; dyspepsia; diminished appetite

RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS

Rhinitis; influenza; cough

NERVOUS SYSTEM DISORDERS

Vertigo/dizziness; paresthesia

SKIN AND SUBCUTANEOUS TISSUE DISORDERS

Pruritus; rash (non-specified); angioedema; urticaria

MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS

Arthralgia including monoarticular; myalgia; back pain; neck pain; shoulder pain; neck stiffness

BLOOD AND LYMPHATIC DISORDERS

Lymphadenopathy

PSYCHIATRIC DISORDERS

Insomnia/disturbed sleep

EAR AND LABYRINTH DISORDERS

Earache

RENAL AND URINARY DISORDERS

Dysuria

CARDIAC DISORDERS

Hypotension

6.2 Post-Marketing Experience

The following additional adverse reactions have been reported with use of the marketed vaccine. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to a vaccine exposure.

Immune System Disorders

Hypersensitivity reactions including anaphylactic/anaphylactoid reactions, bronchospasm, and urticaria have been reported within the first few hours after vaccination. An apparent hypersensitivity syndrome (serum-sickness-like) of delayed onset has been reported days to weeks after vaccination, including: arthralgia/arthritis (usually transient), fever, and dermatologic reactions such as urticaria, erythema multiforme, ecchymoses and erythema nodosum *[see Warnings and Precautions (5.1)]*. Autoimmune diseases including systemic lupus erythematosus (SLE), lupus-like syndrome, vasculitis, and polyarteritis nodosa have also been reported.

Gastrointestinal Disorders

Elevation of liver enzymes; constipation

Nervous System Disorders

Guillain-Barré syndrome; multiple sclerosis; exacerbation of multiple sclerosis; myelitis including transverse myelitis; seizure; febrile seizure; peripheral neuropathy including Bell's Palsy; radiculopathy; herpes zoster; migraine; muscle weakness; hypesthesia; encephalitis

Skin and Subcutaneous Disorders

Stevens-Johnson syndrome; alopecia; petechiae; eczema

Musculoskeletal and Connective Tissue Disorders

Arthritis

Pain in extremity

Blood and Lymphatic System Disorders

Increased erythrocyte sedimentation rate; thrombocytopenia

Psychiatric Disorders

Irritability; agitation; somnolence

Eye Disorders

Optic neuritis; tinnitus; conjunctivitis; visual disturbances; uveitis

Cardiac Disorders

Syncope; tachycardia

The following adverse reaction has been reported with another Hepatitis B Vaccine (Recombinant) but not with RECOMBIVAX HB: keratitis.

7 DRUG INTERACTIONS

7.1 Concomitant Administration with Other Vaccines

Do not mix RECOMBIVAX HB with any other vaccine in the same syringe or vial. Use separate injection sites and syringes for each vaccine.

In clinical trials in children, RECOMBIVAX HB was concomitantly administered with one or more of the following US licensed vaccines: Diphtheria, Tetanus and whole cell Pertussis; oral Poliomyelitis vaccine; Measles, Mumps, and Rubella Virus Vaccine, Live; Haemophilus b Conjugate Vaccine (Meningococcal Protein Conjugate)] or a booster dose of Diphtheria, Tetanus, acellular Pertussis. Safety and immunogenicity were similar for concomitantly administered vaccines compared to separately administered vaccines.

In another clinical trial, a related HBsAg-containing product, Haemophilus b Conjugate (Meningococcal Protein Conjugate) and Hepatitis B (Recombinant) combination product (no longer licensed), was given concomitantly with eIPV (enhanced inactivated Poliovirus vaccine) or VARIVAX® [Varicella Virus Vaccine Live (Oka/Merck)], using separate sites and syringes for injectable vaccines. No serious vaccine-related adverse events were reported, and no impairment of immune response to these individually tested vaccine antigens was demonstrated.

The Haemophilus b Conjugate (Meningococcal Protein Conjugate) and Hepatitis B (Recombinant) combination product (no longer licensed) has also been administered concomitantly with the primary series of DTaP to a limited number of infants. No serious vaccine-related adverse events were reported.

7.2 Concomitant Administration with Immune Globulin

RECOMBIVAX HB may be administered concomitantly with HBIG. The first dose of RECOMBIVAX HB may be given at the same time as HBIG, but the injections should be administered at different sites.

7.3 Interference with Laboratory Tests

Hepatitis B surface antigen (HBsAg) derived from hepatitis B vaccines has been transiently detected in blood samples following vaccination. Serum HBsAg detection may not have diagnostic value within 28 days after receipt of a hepatitis B vaccine, including RECOMBIVAX HB.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4%, and 15% to 20%, respectively.

There are no adequate and well-controlled studies designed to evaluate RECOMBIVAX HB in pregnant women. Available post-approval data do not suggest an increased risk of miscarriage or major birth defects in women who received RECOMBIVAX HB during pregnancy.

Developmental toxicity studies have not been conducted with the vaccine in animals.

Data

Human Data

In post-licensure clinical studies of RECOMBIVAX HB, 26 pregnant women were inadvertently administered RECOMBIVAX HB following their last menstrual period. Among these pregnancies, after excluding elective terminations (n=3), there were 23 pregnancies with known outcomes all with exposure in the first trimester. Miscarriage was reported in 4 of 23 (17%) pregnancies and major birth defects were reported in 0 of 19 (0%) live births. The rates of miscarriage and major birth defects were consistent with estimated background rates.

Post-approval adverse reactions are reported voluntarily from a population of uncertain size. It is not always possible to reliably estimate their frequency or establish a causal relationship to the vaccine.

In prospectively reported spontaneous post-approval reports from 1986 to 2018, 105 women with known pregnancy outcomes were exposed to RECOMBIVAX HB during pregnancy following the last menstrual period. After excluding induced abortions (n=5), those with exposure in the third trimester (n=4), and those with an unknown exposure timing (n=6), there were 90 pregnancies with known outcomes with exposures in the first or second trimester. Miscarriage was reported for 7 of 90 (7.8%) pregnancies. Major birth defects were reported for 2 of 83 (2.4%) live born infants. The rates of miscarriage and major birth defects were consistent with estimated background rates.

8.2 Lactation

Risk Summary

It is not known whether RECOMBIVAX HB is excreted in human milk. Data are not available to assess the effects of RECOMBIVAX HB on the breastfed infant or on milk production/excretion.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for RECOMBIVAX HB and any potential adverse effects on the breastfed child from RECOMBIVAX HB or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to the disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness of RECOMBIVAX HB have been established in all pediatric age groups. Maternally transferred antibodies do not interfere with the active immune

response to the vaccine. *[See Adverse Reactions (6.1) and Clinical Studies (14.1 and 14.2).]* The safety and effectiveness of RECOMBIVAX HB Dialysis Formulation in children have not been established.

8.5 Geriatric Use

Clinical studies of RECOMBIVAX HB used for licensure did not include sufficient numbers of subjects 65 years of age and older to determine whether they respond differently from younger subjects. However, in later studies it has been shown that a diminished antibody response can be expected in persons older than 60 years of age.

11 DESCRIPTION

RECOMBIVAX HB Hepatitis B Vaccine (Recombinant) is a sterile suspension of non-infectious subunit viral vaccine derived from HBsAg produced in yeast cells. A portion of the hepatitis B virus gene, coding for HBsAg, is cloned into yeast, and the vaccine for hepatitis B is produced from cultures of this recombinant yeast strain according to methods developed in the Merck Research Laboratories.

The antigen is harvested and purified from fermentation cultures of a recombinant strain of the yeast *Saccharomyces cerevisiae* containing the gene for the *adw* subtype of HBsAg. The fermentation process involves growth of *Saccharomyces cerevisiae* on a complex fermentation medium which consists of an extract of yeast, soy peptone, dextrose, amino acids and mineral salts. The HBsAg protein is released from the yeast cells by cell disruption and purified by a series of physical and chemical methods. The purified protein is treated in phosphate buffer with formaldehyde and then coprecipitated with alum (potassium aluminum sulfate) to form bulk vaccine adjuvanted with amorphous aluminum hydroxyphosphate sulfate. Each dose contains less than 1% yeast protein. The vaccine produced by the Merck method has been shown to be comparable to the plasma-derived vaccine in terms of animal potency (mouse, monkey, and chimpanzee) and protective efficacy (chimpanzee and human).

The vaccine against hepatitis B, prepared from recombinant yeast cultures, is free of association with human blood or blood products.

RECOMBIVAX HB Hepatitis B Vaccine (Recombinant) is supplied in three formulations. *[See How Supplied/Storage and Handling (16).]*

Pediatric/Adolescent Formulation (Without Preservative), 10 mcg/mL: each 0.5 mL dose contains 5 mcg of hepatitis B surface antigen.

Adult Formulation (Without Preservative), 10 mcg/mL: each 1 mL dose contains 10 mcg of hepatitis B surface antigen.

Dialysis Formulation (Without Preservative), 40 mcg/mL: each 1 mL dose contains 40 mcg of hepatitis B surface antigen.

All formulations contain approximately 0.5 mg of aluminum (provided as amorphous aluminum hydroxyphosphate sulfate, previously referred to as aluminum hydroxide) per mL of vaccine. In each formulation, hepatitis B surface antigen is adsorbed onto approximately 0.5 mg of aluminum (provided as amorphous aluminum hydroxyphosphate sulfate) per mL of vaccine. The vaccine contains <15 mcg/mL residual formaldehyde. The vaccine is of the *adw* subtype.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

RECOMBIVAX HB has been shown to elicit antibodies to hepatitis B virus as measured by ELISA.

Antibody concentrations ≥10mIU/mL against HBsAg are recognized as conferring protection against hepatitis B infection.{2}

Infection with hepatitis B virus can have serious consequences including acute massive hepatic necrosis and chronic active hepatitis. Chronically infected persons are at increased risk for cirrhosis and hepatocellular carcinoma.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

RECOMBIVAX HB has not been evaluated for its carcinogenic or mutagenic potential, or its potential to impair fertility *[see Use in Specific Populations (8)]*.

14 CLINICAL STUDIES

14.1 Efficacy in Neonates with Peripartum Exposure to Hepatitis B

The protective efficacy of three 5 mcg doses of RECOMBIVAX HB has been demonstrated in neonates born of mothers positive for both HBsAg and HBeAg (a core-associated antigenic complex which correlates with high infectivity). In a clinical study of infants who received one dose of HBIG at birth followed by the recommended three-dose regimen of RECOMBIVAX HB, chronic infection had not occurred in 96% of 130 infants after nine months of follow-up.{4} The estimated efficacy in prevention of chronic hepatitis B infection was 95% as compared to the infection rate in untreated historical controls.{5} Significantly fewer neonates became chronically infected when given one dose of HBIG at birth followed by the recommended three-dose regimen of RECOMBIVAX HB when compared to historical controls who received only a single dose of HBIG.{6} As demonstrated in the above study, HBIG, when administered simultaneously with RECOMBIVAX HB at separate body sites, did not interfere with the induction of protective antibodies against hepatitis B virus elicited by the vaccine.{6}

14.2 Immunogenicity of a Three-Dose Regimen in Healthy Infants, Children, and Adolescents

Three 5 mcg doses of RECOMBIVAX HB induced a protective level of antibody in 100% of 92 infants, 99% of 129 children, and in 99% of 112 adolescents *[see Dosage and Administration (2.3)].*

14.3 Immunogenicity of a Two-Dose Regimen in Healthy Adolescents 11 through 15 Years of Age

For adolescents (11 through 15 years of age), the immunogenicity of a two-dose

regimen (10 mcg at 0 and 4-6 months) was compared with that of the standard three-dose regimen (5 mcg at 0, 1, and 6 months) in an open, randomized, multicenter study. The proportion of adolescents receiving the two-dose regimen who developed a protective level of antibody one month after the last dose (99% of 255 subjects) appears similar to that among adolescents who received the three-dose regimen (98% of 121 subjects). After adolescents (11 through 15 years of age) received the first 10-mcg dose of the two-dose regimen, the proportion who developed a protective level of antibody was approximately 72%.

14.4 Immunogenicity in Healthy Adults

Clinical studies have shown that RECOMBIVAX HB when injected into the deltoid muscle induced protective levels of antibody in 96% of 1213 healthy adults who received the recommended three-dose regimen. Antibody responses varied with age; a protective level of antibody was induced in 98% of 787 young adults 20-29 years of age, 94% of 249 adults 30-39 years of age and in 89% of 177 adults ≥40 years of age.

14.5 Efficacy and Immunogenicity in Specific Populations

Chronic Hepatitis C Infection

In one published study, the seroprotection rates in individuals with chronic hepatitis C virus (HCV) infection given the standard regimen of RECOMBIVAX HB was approximately 70%.{7} In a second published study of intravenous drug users given an accelerated schedule of RECOMBIVAX HB, infection with HCV did not affect the response to RECOMBIVAX HB.{8}

Predialysis and Dialysis Adult Patients

Predialysis and dialysis adult patients respond less well to hepatitis B vaccines than do healthy individuals; however, vaccination of adult patients early in the course of their renal disease produces higher seroconversion rates than vaccination after dialysis has been initiated.{9} In addition, the responses to these vaccines may be lower if the vaccine is administered as a buttock injection. When 40 mcg of Hepatitis B Vaccine (Recombinant), was administered in the deltoid muscle, 89% of 28 participants developed anti-HBs with 86% achieving levels ≥10 mIU/mL. However, when the same dosage of this vaccine was administered inappropriately either in the buttock or a combination of buttock and deltoid, 62% of 47 participants developed anti-HBs with 55% achieving levels of ≥10 mIU/mL.

15 REFERENCES

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9. Recommendations of the Advisory Committee on Immunization Practices (ACIP): Hepatitis B Virus Infection: A Comprehensive Strategy to Eliminate Transmission in the United States, 1996 update, MMWR (draft January 13, 1996).

16 HOW SUPPLIED/STORAGE AND HANDLING

Product: 50090-1716

17 PATIENT COUNSELING INFORMATION

Information for Vaccine Recipients and Parents/Guardians

- Inform the patient, parent or guardian of the potential benefits and risks associated with vaccination, as well as the importance of completing the immunization series.
- Question the vaccine recipient, parent or guardian about the occurrence of any symptoms and/or signs of adverse reaction after a previous dose of hepatitis B vaccine.
- Tell the patient, parent or guardian to report adverse events to the physician or clinic where the vaccine was administered.
- Prior to vaccination, give the patient, parent or guardian the Vaccine Information Statements which are required by the National Vaccine Injury Act of 1986. The materials are available free of charge at the Centers for Disease Control and Prevention (CDC) website (www.cdc.gov/vaccines).
- Tell the patient, parent or guardian that the United States Department of Health and Human Services has established a Vaccine Adverse Event Reporting System (VAERS) to accept all reports of suspected adverse events after the administration of any vaccine, including but not limited to the reporting of events by the National Childhood Vaccine Injury Act of 1986. The VAERS toll-free number is 1-800-822-7967. Reporting forms may also be obtained at the VAERS website at (www.vaers.hhs.gov).

Manuf. and Dist. by: Merck Sharp & Dohme Corp., a subsidiary of **MERCK & CO., INC.,**

Whitehouse Station, NJ 08889, USA

For patent information: www.merck.com/product/patent/home.html

uspi-v232-i-2002r442

Hepatitis B Vaccine (Recombinant)

RECOMBIVAX HB

hepatitis b vaccine (recombinant) injection, suspension

Product Information			
Product Type	VACCINE	**Item Code (Source)**	NDC:50090-1716(NDC:0006-4981)
Route of Administration	INTRAMUSCULAR, SUBCUTANEOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
HEPATITIS B VIRUS SUBTYPE ADW HBSAG SURFACE PROTEIN ANTIGEN (UNII: XL4HLC6JH6) (HEPATITIS B VIRUS SUBTYPE ADW HBSAG SURFACE PROTEIN ANTIGEN - UNII:XL4HLC6JH6)	HEPATITIS B VIRUS SUBTYPE ADW HBSAG SURFACE PROTEIN ANTIGEN	5 ug in 0.5 mL

Other Ingredients		
Ingredient Kind	**Ingredient Name**	**Quantity**
ADJV	**ALUMINUM HYDROXYPHOSPHATE SULFATE** (UNII: F41V936QZM)	0.25 mg in 0.5 mL

Product Characteristics			
Color	WHITE (slightly opaque, white)	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:50090-1716-0	10 in 1 POUCH		
1	NDC:50090-1716-9	.5 mL in 1 VIAL, SINGLE-DOSE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA101066	07/23/1986	

Labeler - A-S Medication Solutions (830016429)

Establishment

Name	Address	ID/FEI	Business Operations
A-S Medication Solutions		830016429	RELABEL(50090-1716)

Revised: 6/2021 A-S Medication Solutions